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10/643,502	08/19/2003	Yunping Huang	32993-72726	5516

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EXAMINER

MAIER, LEIGH C

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/643,502

Applicant(s)

HUANG ET AL.

Examiner

Leigh C. Maier

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 8/30/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite “derivatives having a *common* covalently bound label.” (emphasis added) The term “common covalently bound label” has no particular art-accepted meaning, and the specification does not provide a definition describing the metes and bounds of this limitation. The claims are thus rendered vague and indefinite.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9-11, 16, 21, 22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over RADEMAKER et al (Anal. Biochem., 1998) and STUBBS et al (Anal. Biochem., 1997) in view of PAREKH et al (US 6,180,779) and BLIXT et al (Carbohydr. Res., 1999).

The claims are drawn to a method for preparing oligosaccharides from a glycoprotein comprising contacting the glycoprotein with an aqueous solution of ammonium hydroxide and ammonium carbonate. Dependents add steps of labeling and fractionating the resulting oligosaccharides and/or contacting them with aqueous acid, which may be boric acid.

RADEMAKER teaches the cleavage of glycans (oligosaccharides) from a glycopeptide by contacting the glycopeptide with ammonium hydroxide. See abstract. The focus of the reference is the analysis of the resulting peptide. However, the reference does recognize the importance of a method for isolating and analyzing the oligosaccharides resulting from such a process. See first paragraph of the reference at page 149. The reference also discusses the known “peeling” side reaction that occurs when the reducing oligosaccharide remains exposed to alkaline reaction conditions. This can be avoided by the use of a reductant, but a reductant can degrade some of the peptides as well as produce an alditol rather than a reducing oligosaccharide. See the paragraph bridging the columns at page 152. The reference also teaches that the amount of ammonium hydroxide must be adjusted relative to the amount of NaOH that is

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typically used because the former is a weaker base. However, the substitution of ammonium hydroxide has the advantage of eliminating the need for desalting. See page 152, right column, first full paragraph. The reference does not teach the use of ammonium carbonate or further processing of the oligosaccharides.

STUBBS teaches that the treatment of an oligosaccharide with ammonium bicarbonate results in a glycosylamine oligosaccharide, which is stable in alkaline conditions. The reference further teaches covalent labeling of the glycosylamine oligosaccharide and HPLC separation of the oligosaccharides. See abstract and Fig. 1-3. The labeled oligosaccharides can be converted to reducing oligosaccharides with acid cleavage, and these oligosaccharides can also be separated by HPLC. See page 359, right column, middle paragraph and page 362, paragraph bridging the two columns.

PAREKH further discusses the lability of reducing oligosaccharides and the “peeling” reaction. See Fig 2 and col 2, lines 12-34. The reference also discusses the desirability of isolating and analyzing oligosaccharides that are released from a glycoprotein/peptide, as these oligosaccharides “are increasingly recognized as important biological molecules in their own right.” See col 1, lines 24-41.

BLIXT teaches the preparation of glycosylamines from reducing oligosaccharides by treatment with ammonia/ammonium bicarbonate. See Scheme 1. The reference further teaches hydrolyzing glycosylamines back to reducing oligosaccharides by reducing the pH with sodium borate. See page 83, first full paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the procedure of RADEMAKER by the addition of a reactant that

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would create conditions to stabilize the resulting oligosaccharide or transform it to a stable entity. STUBBS and BLIXT had taught that ammonium bicarbonate or ammonia/ammonium bicarbonate converts a reducing oligosaccharide to a glycosylamine, so one of ordinary skill would be motivated to add a bicarbonate to the ammonium hydroxide in order to prepare this stable entity. RADEMAKER teaches that the oligosaccharide cleavage requires a strong base, so one of ordinary skill would be motivated to substitute ammonium carbonate in order to provide a higher pH buffer system/reaction mixture. The resulting aqueous solution would comprise carbonate and bicarbonate ions. One of ordinary skill would reasonably expect these reaction conditions to (1) cleave oligosaccharides from a glycoprotein and (2) provide a stable glycosylamine. RADEMAKER describes removing the reactants by evaporation. The addition of a carbonate would simply add another volatile reactant, so removal of reactants by evaporation would be obvious to one of ordinary skill.

It would be obvious to one of ordinary skill to further manipulate the resulting glycosylamine by (1) covalent labeling, such as that seen in STUBBS, for separation or oligosaccharides or (2) hydrolysis to prepare a stable reducing oligosaccharide for structural analysis or biological use, as taught by PAREKH. Regarding hydrolysis, BLIXT teaches the use of sodium borate to adjust pH, but it would be obvious to one of ordinary skill to substitute boric acid to maintain a volatile reaction mixture and obviate the need for desalting.

Finally, it would be obvious to separate any of the desired reaction products from the reactants and/or by-products, including the de-glycosylated protein.

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Claims 12-15 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over RADEMAKER et al (Anal. Biochem., 1998) and STUBBS et al (Anal. Biochem., 1997) in view of PAREKH et al (US 6,180,779) and BLIXT et al (Carbohydr. Res., 1999) as applied to claims 1-11, 16, 21, 22, and 24 above, and further in view of JACKSON (US 5,340,453).

The invention is as set forth above. Dependents are drawn to covalent labeling of reduced oligosaccharides and separation of said labeled oligosaccharides.

RADEMAKER, STUBBS, PAREKH, and BLIXT teach as set forth above. The references do not teach covalent labeling of reducing oligosaccharides or separation of said labeled oligosaccharides.

JACKSON teaches labeling reducing oligosaccharides for separation and analysis. See abstract and figures.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare reducing oligosaccharides by hydrolyzing glycosylamines, as discussed above. It would be further obvious to modify said oligosaccharides through covalent attachment of a detectable label, such as that taught by JACKSON, with a reasonable expectation of success. The artisan would be motivated to do so as a method for separating and analyzing the oligosaccharides derived in the process discussed above. It would be within the scope of the artisan to select any known method of doing so.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over RADEMAKER et al (Anal. Biochem., 1998) and STUBBS et al (Anal. Biochem., 1997) in view of PAREKH et

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al (US 6,180,779) and BLIXT et al (Carbohydr. Res., 1999) as applied to claims 1-11, 16, 21, 22, and 24 above, and further in view of RAUSCHER et al (US 5,108,913).

The invention is as set forth above. Claim 23 requires separation of the boric acid by evaporation of a methanol solution.

RADEMAKER, STUBBS, PAREKH, and BLIXT teach as set forth above. The references do not teach separation of the boric acid by evaporation of a methanol solution.

The addition of methanol followed by evaporation is a known method for the removal of boric acid. See RAUSCHER at example 6.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify RADEMAKER as discussed above. It would be further obvious to remove any residual boric acid used in hydrolyzing glycosylamines by addition of methanol followed by evaporation. The method is known in the art, so the artisan would reasonably expect success in employing this procedure.

***Examiner's hours, phone & fax numbers***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-930692.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more. Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the

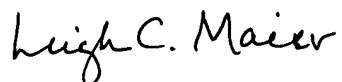


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PAIR system, see <http://pair-direct.uspto.gov> Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

A handwritten signature in black ink that reads "Leigh C. Maier". The signature is written in a cursive, flowing style.

Leigh C. Maier  
Primary Examiner  
July 8, 2005